Amendments to the Claims

1. (Currently Amended) A method for making a prognosis of disease course in a human breast or prostate cancer patient, the method comprising the step of:

    (a) obtaining a sample of a tumor from the human cancer patient;

    (b) determining a level of nuclear localization of p53 protein in the tumor sample and comparing the level of nuclear localization of p53 protein in the tumor sample with the level of nuclear localization of p53 protein in a non-invasive, non-metastatic tumor sample;

    (c) determining a level of thrombospondin 1 expression in the tumor sample and comparing the level of thrombospondin 1 expression in the tumor sample with the level of thromobospoin 1 expression in a non-invasive, non-metastatic tumor sample;

    (d) determining by immunohistochemistry an extent of microvascularization in the tumor sample and comparing the extent of microvascularization in the tumor sample with the extent of microvascularization in a non-invasive, non-metastatic tumor sample; and

    (e) preparing a prognostic index comprising the results of the determination of the levels of nuclear localization of p53, thrombospondin 1 expression, and the extent of microvascularization in the tumor sample,

wherein said prognosis is predicted from considering a likelihood of further neoplastic disease which is made when the level of nuclear localization of p53 protein in the tumor sample is [[~~great~~]] **greater** than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample; the level of thrombospondin 1 expression in the tumor sample is less than the level of thromobospondin 1 expression in the non-invasive, non-metastatic tumor sample; and the extent of microvascularization in the tumor sample is greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

2. (Original) The method of Claim 1, wherein the level of nuclear localization of p53 protein in the tumor sample is from about twofold to about tenfold greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample.

3. (Original) The method of Claim 1, wherein the level of thrombospondin 1 expression in the tumor sample is from about twofold to about tenfold less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample.

4. (Original) The method of Claim 1, wherein the extent of microvascularization in the tumor sample is from about twofold to about tenfold greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

5. (Original) The method of Claim 1, wherein the level of nuclear localization of p53 protein in the tumor sample is from about twofold to about tenfold greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample, and wherein the level of thrombospondin 1 expression in the tumor sample is from about twofold to about tenfold less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample and wherein the extent of microvascularization in the tumor sample is from about twofold to about tenfold greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

6. (Original) The method of Claim 1, wherein the level of nuclear localization of p53 protein in the tumor sample is from about fivefold greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample, and wherein the level of thrombospondin 1 expression in the tumor sample is from about fivefold less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample and wherein the extent of microvascularization in the tumor sample is from about sixfold greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

7. (Original) The method of Claim 1, wherein the level of nuclear localization of p53, the level of thrombospondin 1 expression and the extent of microvascularization are determined by immunohistochemical staining

8. (Original) The method of Claim 1 wherein the cancer is breast cancer.

9. (Original) The method of Claim 1 wherein the cancer is prostrate cancer.

10. (Cancelled)

11. (Withdrawn) A method for making a prognosis of disease course in a human cancer patient, the method comprising the steps of:

(a) obtaining a sample of a tumor from the human cancer patient;

(b) determining a level of nuclear localization of p53 protein in the tumor sample and comparing the level of nuclear localization of p53 protein in the tumor sample with the level of nuclear localization of p53 protein in a non-invasive, non-metastatic tumor sample;

(c) determining a level of thrombospondin 1 expression in the tumor sample and comparing the level of thrombospondin 1 expression in the tumor sample with the level of thrombospondin 1 expression in a non-invasive, non-metastatic tumor sample;

(d) determining by immunohistochemistry an extent of microvascularization in the tumor sample and comparing the extent of microvascularization in the tumor sample with the extent of microvascularization in a non-invasive, non-metastatic tumor sample; and

(e) preparing an index comprising

(i) the product of the percentage of cells in the tumor sample that are positive for nuclear localization of p53 protein multiplied by the sum of (one plus the intensity of immunohistochemical staining);

(ii) the product of the percentage of cells in the tumor sample that are positive for microvascularization multiplied by the sum of (one plus the intensity of immunohistochemical staining); and

(iii) the product of the percentage of cells in the tumor sample that are positive for thrombospondin 1 expression multiplied by the sum of (one plus the intensity of immunohistochemical staining);

wherein for steps (e)(I) and (e)(ii) the intensity of staining is assigned a value of 0 for staining equal to a negative control, a value of 1 for weak staining greater than the negative control, a value of 2 for moderate staining intensity, a value of 3 for staining intensity equal to a positive control, and a value of 4 for staining intensity greater than the positive control, and wherein for step (e)(iii) the intensity of staining is assigned a value of 4 for staining equal to or greater than a negative control, a value of 3 for staining slightly decreased from the negative control, a value of 2 for staining intensity moderately decreased from the negative control, a value of 1 for staining intensity equal to a positive control, and a value of 0 for staining intensity less than the positive control, and a value of 0 for staining less than the positive control; wherein the products of steps (e)(I), (e)(ii) and (e)(iii) are weighted on a scale from +1 to --4 and wherein the index comprises the sum of the weighted products for nuclear localization of p53, thrombospondin 1 expression and microvascularization, wherein a prognosis of a likelihood of further neoplastic disease is made when said sum is -5 or less, wherein said prognosis is predicted from considering a likelihood of further neoplastic disease which is made when the level of nuclear localization of in the tumor sample is greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample; the level of thrombospondin 1 expression in the tumor sample is less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample; and the extent of microvascularization in the tumor sample is greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

12. (Withdrawn) The method of Claim 11 wherein the index has a value of -5, -6, -7 or -8.

13. (Withdrawn) The method of Claim 11 wherein the cancer is breast cancer.

14. (Withdrawn) The method of Claim 11 wherein the cancer is prostate cancer.

15. (Withdrawn) The method of Claim 11 wherein the cancer is melanoma.

16. (Withdrawn) The method of Claim 1, wherein the prognosis of disease course includes a risk for metastasis, recurrence and relapse of neoplastic disease.

17. (Withdrawn) The method of Claim 1, wherein the prognosis of disease course includes staging malignant disease in a human cancer patient.

18. (Withdrawn) The method of Claim 11, wherein the prognosis of disease course includes a risk for metastasis, recurrence and relapse of neoplastic disease.

19. (Withdrawn) The method of Claim 11, wherein the prognosis of disease course includes staging malignant disease in a human cancer patient.

20. (Withdrawn) The method of Claim 1, wherein the prognostic index is produced by preparing a weighted scale of expression levels of the tumor markers related to progression observed in a representative sample of a particular tumor type, wherein the different values in the weighted scale are related to increased invasiveness or metastatic spread in the representative sample.